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Global attractivity in a model of genetic regulatory system with delay ☆

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ABSTRACT

A model of genetic regulatory system with delay is considered, and it is proved that under certain conditions the model has a unique constant equilibrium which is globally attractive. This result limits the parameter space for which oscillations are possible.

1. Introduction

In [5], Smolen et al. proposed the following delayed differential equations to model genetic regulatory system:

$$\begin{cases} \frac{d[TF-A]}{dt} = \left\{\frac{k_{1,f}[TF-A]^2}{[TF-A]^2+K_{1,d}(1+[TF-R]/K_{R,d})}\right\}(t-\tau) - k_{1,d}[TF-A] + r, \\ \frac{d[TF-R]}{dt} = \left\{\frac{k_{2,f}[TF-A]^2}{[TF-A]^2+K_{2,d}(1+[TF-R]/K_{R,d})}\right\}(t-\tau) - k_{2,d}[TF-R], \end{cases} \tag{1.1}$$

where $[TF-A]$ and $[TF-R]$ denote the concentrations of transcription factors $TF-A$ and $TF-R$, respectively. Here parameters $k_{i,f}, k_{i,d}, K_{i,d}$, $(i=1,2)$, r and $K_{R,d}$ are all positive constants, and the delay $\tau > 0$ is the time between transcription and appearance of functional protein. More detailed explanation of the above model can be found in [4,5]. It was shown numerically that delay could induce oscillations for system (1.1), (see reference [5]). Then in [6], Wan and Zou analyzed Hopf bifurcation of system (1.1), and their results implied that the delay could induce oscillations. For convenience, letting

$$x = [TF-A], \quad y = [TF-R], \quad K_{R,d} = q \quad \text{and} \quad k_i = k_{i,f}, \quad p_i = K_{i,d}, \quad l_i = k_{i,d}, \text{ for } i = 1,2,$$

we analyzed the model in the following form:

$$\begin{cases} \frac{dx}{dt} = \frac{k_1 x(t-\tau)^2}{x(t-\tau)^2+p_1(1+y(t-\tau)/q)} - l_1 x(t) + r, \\ \frac{dy}{dt} = \frac{k_2 x(t-\tau)^2}{x(t-\tau)^2+p_2(1+y(t-\tau)/q)} - l_2 y(t). \end{cases} \tag{1.2}$$

There are also many results about stability and bifurcations on other gene regulatory network models, (see references [1,7,8]).

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In this note, we prove that in some parameter regions the constant positive equilibrium of system (1.2) is globally attractive through upper and lower solutions methods. Hence our result implies that delay-induced oscillations could occur only when the parameters are out of these regions.

2. Main results

We consider system (1.2) with the following initial condition:

$$x(s) = x_0(s) \geq 0 \quad y(s) = y_0(s) \geq 0, \quad s \in [-\tau, 0], \tag{2.1}$$

where $x_0(0), y_0(0) > 0$, and $x_0(s), y_0(s) \in C([-\tau, 0], \mathbb{R})$. Then we have the following results on the global existence of the solution of system (1.2) and (2.1).

Lemma 2.1. *Assume that the parameters q, r, τ, and $k_i, l_i, p_i (i = 1, 2)$ are all positive. Then for any initial value $x_0(s), y_0(s) \geq 0$, where $x_0(0), y_0(0) > 0$, system (1.2) has a unique positive solution $(x(t), y(t))$ exists on $[-\tau, \infty)$.*

Proof. From the variation-of-constants formula, we have

$$\begin{aligned} x(t) &= e^{-l_1 t} x_0(0) + \int_0^t e^{-l_1(t-s)} \left[\frac{k_1 x_0(s-\tau)^2}{x_0(s-\tau)^2 + p_1(1 + y_0(s-\tau)/q)} + r \right] ds, \\ y(t) &= e^{-l_2 t} y_0(0) + \int_0^t e^{-l_2(t-s)} \left[\frac{k_2 x_0(s-\tau)^2}{x_0(s-\tau)^2 + p_2(1 + y_0(s-\tau)/q)} \right] ds \end{aligned} \tag{2.2}$$

for $t \in [0, \tau]$. Since $x_0(s), y_0(s) \geq 0$ and $x_0(0), y_0(0) > 0$, Eq. (2.2) yields $x(t), y(t) > 0$ for $t \in [0, \tau]$. Then by the method of steps we can prove the lemma. □

In the following, we mainly focus on the global attractivity of the equilibrium of system (1.2). The proof is based on the upper and lower solutions method in [2,3]. First, we show that any solution of system (1.2) is attracted by an invariant rectangular region.

Lemma 2.2. *Suppose that the parameters q, r, τ, and $k_i, l_i, p_i (i = 1, 2)$ are all positive. Choose a constant ϵ_0 so that*

$$0 < \epsilon_0 < \min\left\{ \frac{r}{2l_1}, \frac{k_2 r^2}{r^2 l_2 + 4 l_1^2 l_2 p_2 \left[1 + \left(\frac{k_2}{l_2} + \frac{r}{2l_1}\right)/q\right]} \right\}$$

and define

$$\bar{c}_1 = \frac{k_1 + r}{l_1} + \epsilon_0, \quad \underline{c}_1 = \frac{r}{l_1} - \epsilon_0, \quad \bar{c}_2 = \frac{k_2}{l_2} + \epsilon_0, \quad \underline{c}_2 = \frac{k_2 \underline{c}_1^2}{l_2[\underline{c}_1^2 + p_2(1 + \bar{c}_2/q)]} - \epsilon_0.$$

Then this chosen positive $\underline{c}_i, \bar{c}_i (i = 1, 2)$, satisfy

$$\begin{aligned} &\tfrac{k_1 \bar{c}_1^2}{\bar{c}_1^2 + p_1(1 + \underline{c}_2/q)} - l_1 \bar{c}_1 + r \leq 0, \quad \tfrac{k_2 \bar{c}_1^2}{\bar{c}_1^2 + p_2(1 + \underline{c}_2/q)} - l_2 \bar{c}_2 \leq 0, \\ &\tfrac{k_1 \underline{c}_1^2}{\underline{c}_1^2 + p_1(1 + \bar{c}_2/q)} - l_1 \underline{c}_1 + r \geq 0, \quad \tfrac{k_2 \underline{c}_1^2}{\underline{c}_1^2 + p_2(1 + \bar{c}_2/q)} - l_2 \underline{c}_2 \geq 0 \end{aligned} \tag{2.3}$$

and for any initial value $x_0(s), y_0(s) \geq 0$, where $x_0(0), y_0(0) > 0$, there exists $t_0 > 0$ such that the corresponding solution $(x(t), y(t))$ satisfies

$$(\underline{c}_1, \underline{c}_2) \leqslant (x(t), y(t)) \leqslant (\bar{c}_1, \bar{c}_2)$$

for any $t > t_0(\phi)$.

Proof. It can be easy to verify that $\underline{c}_i, \bar{c}_i (i = 1, 2)$ are positive, and satisfy Eq. (2.3). Then we only need to prove that the solution of system (1.2) is attracted by an invariant rectangular region. Since $x(t)$ satisfies

$$\begin{aligned} \frac{dx}{dt} &= \frac{k_1 x(t-\tau)^2}{x(t-\tau)^2 + p_1(1 + y(t-\tau)/q)} - l_1 x(t) + r \geqslant r - l_1 x \quad \text{and} \\ \frac{dx}{dt} &= \frac{k_1 x(t-\tau)^2}{x(t-\tau)^2 + p_1(1 + y(t-\tau)/q)} - l_1 x(t) + r \leqslant k_1 + r - l_1 x, \end{aligned}$$